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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/054,710	01/22/2002	Koichi Masuda	047940-0119	5419

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/054,710	MASUDA ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *15,16,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,17-30,33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on October 4, 2004 has been received and entered into the case. Claims 1 – 35 are pending; claims 15 – 16 and 31 – 32 are withdrawn from consideration; claims 1 – 14, 17 – 30 and 33 – 35have been considered on the merits. All arguments have been fully considered.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1 – 8, 10, 14, 17 – 24, 26, 29 – 30 and 33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kai in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the agents have on the ECT or cells thereof; wherein the matrix is cultured to be rapidly degraded losing about half of its proteoglycan content within 24 hours when treated withIL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan, collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II, IX, XI, hyaluronan, and at least about 5 mg/cc3 aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium, the measuring is performed without addition of extrinsic radioactivity and the method

further comprises identifying one or more test agents that have desirable characteristics and producing the agents as a therapeutic drug. The modulator of the ECT tissue is a matrix stimulating agent, cytokine or TNF-alpha wherein the cytokine is interleukin 1 (IL-1).

Kai teaches a method for determining effects of agents on cartilage, wherein the cartilage is cultured with IL-1 or TNF, is contacted with the test agent, and is measured for effects of the test agent (abstract). The method is used to screen for therapeutic agents (abstract).

Kai does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc3 aggrecan, a ratio of aggrecan to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to culture the cartilage of Kai using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common culture practices in the art to culture the cartilage of Kai via the methods of Masuda with a reasonable expectation for successfully determining the effects of test agents on cartilage cultures. Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or

intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

4. Claims 1 – 10, 14, 17 – 26, 33 and 35 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Purchio in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the agents have on the ECT or cells thereof; wherein the matrix is cultured to be rapidly degraded losing about half of its proteoglycan content within 24 hours when treated withIL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan, collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II, IX, XI, hyaluronan, and at least about 5 mg/cc3 aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated

chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium, the measuring comprises measuring the amount of proteoglycan in the ECT, is performed without addition of extrinsic radioactivity and the method further comprises identifying one or more test agents that have desirable characteristics and producing the agents as a therapeutic drug. The culturing of ECT and the contacting the cells with the test agent occurs in the same well of a multi-well plate.

Purchio teaches methods for screening effects of test agents on cartilage cultures wherein the cultures are exposed to the test agents and the effects are measured (col.16 line 12-22). Examples of such effects include the amount of proteoglycan (col.16 line 27-34). Specifically, chondrocytes are harvested from articular cartilage and cultured in multi-well plates (col.21 lines 18-60) and the test agents are identified for therapeutic and/or pharmaceutical compounds (col. 16). Purchio teaches that the chondrocytes can be isolated from articular or costal cartilage (col.11 line 62-65).

Purchio does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc3 aggrecan, a ratio of aggrecan to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from

articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to culture the cartilage of Purchio using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common culture practices in the art to culture the cartilage of Purchio via the methods of Masuda with a reasonable expectation for successfully determining the effects of test agents on cartilage cultures. Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

5. Claims 1 – 8, 17 – 24, 29 – 30 and 35 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Saito in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the agents have on the ECT or cells thereof; wherein the matrix is cultured to be rapidly degraded losing about half of its proteoglycan content within 24 hours when treated withIL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic

cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan, collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II, IX, XI, hyaluronan, and at least about 5 mg/cc3 aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium. The modulator of the ECT tissue is a matrix stimulating agent, cytokine or TNF-alpha wherein the cytokine is interleukin 1 (IL-1). Finally, the culturing and contacting step occur in the same well of a multi well plate.

Saito teaches culturing cartilage in multi well plates in the presences of IL-1 alpha, wherein the effects of the test agent were measured (p.727).

Saito does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc3 aggrecan, a ratio of aggrecan

to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to culture the cartilage of Saito using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common culture practices in the art to culture the cartilage of Saito via the methods of Masuda with a reasonable expectation for successfully determining the effects of test agents on cartilage cultures. Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

6. Claims 1 – 11, 17 – 27 and 29 – 30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Huch in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the agents have on the ECT or cells thereof; wherein the matrix is cultured to be rapidly degraded

losing about half of its proteoglycan content within 24 hours when treated withIL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan, collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II, IX, XI, hyaluronan, and at least about 5 mg/cc3 aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium, the measuring comprises measuring the amount of proteoglycan in the ECT, enzymatically degrading the ECT and is performed without addition of extrinsic radioactivity. The method further comprises identifying one or more test agents that have desirable characteristics and producing the agents as a therapeutic drug. The culturing of ECT and the contacting the cells with the test agent occurs in the same well of a multi-well plate. The modulator of the ECT tissue is a matrix stimulating agent, cytokine or TNF-alpha wherein the cytokine is interleukin 1.

Huch teaches methods for culturing articular chondrocytes in an alginate medium in the presence of a test agent, IL-1, wherein proteoglycan was measured (abstract). Specifically, the cartilage was degraded with enzymes, the chondrocytes were cultured with alginate in a multi-well plate in the presence of IL-1, and the amount of proteoglycan was measured (p. 2158).

Huch does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc3 aggrecan, a ratio of aggrecan to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to culture the cartilage of Huch using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common culture practices in the art to culture the cartilage of Huch via the methods of Masuda with a reasonable expectation for successfully determining the effects of test agents on cartilage cultures. Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time

of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

7. Claims 1 – 8, 10, 14, 17 – 24, 26 and 33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lansbury in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the agents have on the ECT or cells thereof; wherein the matrix is cultured to be rapidly degraded losing about half of its proteoglycan content within 24 hours when treated withIL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan, collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II, IX, XI, hyaluronan, and at least about 5 mg/cc3 aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal,

epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium, the measuring is performed without addition of extrinsic radioactivity and the method further comprises identifying one or more test agents that have desirable characteristics and producing the agents as a therapeutic drug.

Lansbury teaches methods for screening the effects of agents on cartilage cultures wherein a chondrocyte cell culture is incubated (or contacted) with the test agent and the effects are measured (claim 34). The method is used to identify agents with desirable, therapeutic characteristics, specifically the ability to repair damaged cartilage (claim 34).

Lansbury does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc3 aggrecan, a ratio of aggrecan to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to culture the cartilage of Lansbury using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by

common culture practices in the art to culture the cartilage of Lansbury via the methods of Masuda with a reasonable expectation for successfully determining the effects of test agents on cartilage cultures. Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

Response to Arguments

Applicant argues that the cartilage of Masuda does not rapidly degrade as claimed; that the degradation rate is not an inherent property of the cartilage of Masuda; that the Examiner must provide rationale for inherency; that applicant has recognized a previously unappreciated trait in the engineered cartilage tissues of Masuda; and that the references do not teach the method of culturing cartilage. Applicant further argues that the references do not teach a method for screening test agents and that there is no suggestion or motivation to combine the references. Finally applicant argues that there is no evidence that the claimed method is "common culture practices" as argued by examiner, who appears to take official notice.

However, these arguments fail to persuade for the following reasons.

Regarding applicant's assertions that the instant cartilage tissue is different from that of Masuda, it is noted that applicant expressly states: "Applicants have recognized a previously unappreciated trait found in select samples of engineered cartilage tissues disclosed by Masuda

et al." In the instant case it is unequivocal that the engineered cartilage tissue of applicant's claims is cultured under the same conditions as disclosed in the prior art. Because the same culture conditions are used to make the engineered tissues, the resulting properties of that tissue must necessarily be the same as disclosed by applicant. Otherwise applicant's invention could not function as disclosed. MPEP § 2112 clearly states: "The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness".

Regarding applicant's assertion that a new trait has been discovered in the cartilage tissues of Masuda, "the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency) (MPEP 2112)

Regarding applicant's arguments that the references do not teach a method for determining the effects of test agents on engineered cartilage tissues, the above rejections specifically identify the references wherein they teach such screening methods. Specifically, Kai teaches a method for determining effects of agents on cartilage that is used to screen for therapeutic agents (abstract); Purchio teaches methods for screening effects of test agents on cartilage cultures wherein the cultures are exposed to the test agents and the effects are measured (col.16 line 12-22); Saito teaches culturing cartilage wherein the effects of test agents are measured (p.727); Huch teaches methods for culturing chondrocytes in the presence of a test agent wherein the effects are measures (p.1258); and Lansbury teaches methods for screening the effects of agents on cartilage cultures claim 34). As such, at the time of the claimed invention, one of ordinary skill in the art would certainly be motivated to use engineered cartilage tissue in the methods of the cited references. While the references do not teach the tissues cultured in the manner claimed, Masuda teaches engineered cartilage tissues that are cultured under the claimed conditions. Moreover, as evidenced by Masuda, the claimed method of culturing cartilage tissue was known in the art (or was "common culture practices"). It is noted that Masuda is evidence that the claimed culture practices were known in the art at the time the claimed invention was made.

Regarding applicant's assertion that the examiner takes official notice or does not provide evidence of "common culture practices", applicant is directed to Masuda. The claimed method of culturing engineered cartilage tissue considered common culture practices as evidenced and taught by Masuda.

Therefore, since the references clearly teach methods for determining effects of test agents on engineered cartilage tissue, and the method of culturing such engineered cartilage tissues is disclosed by Masuda, the claims stand rejected as being obvious for these reasons and those stated in the rejections above.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 571-272-0915. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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December 14, 2004
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